



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,730	11/28/2000	Paul D. Grossman	443D1	7771

22896 7590 12/17/2002
MILA KASAN, PATENT DEPT.
APPLIED BIOSYSTEMS
850 LINCOLN CENTRE DRIVE
FOSTER CITY, CA 94404

EXAMINER

EINSMANN, JULIET CAROLINE

ART UNIT	PAPER NUMBER
----------	--------------

1634

DATE MAILED: 12/17/2002

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/724,730

Applicant(s)

GROSSMAN, PAUL D.

Examiner

Juliet C Einsmann

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 16.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. This action is written in response applicant's correspondence submitted 10/9/02, paper number 15. Claim 1 has been amended. Claims 1-12 are pending. Applicant's amendments and arguments have been thoroughly reviewed but are not persuasive. New rejections are set forth. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the new limitation of "that is designed not to hybridize to said adjacent sequence regions when the first target-specific portion is sequence specifically hybridized to the first target nucleic acid sequence" in claim 1 appears to represent new matter. Applicant argues that basis for this limitation is found in figure 4C. Figure 4C demonstrates complexes as claimed hybridized to target sequences. Figure 4C does not, however discuss or provide basis for what the negative limitation wherein the target specific portion is designed not

to hybridize to any sequence in particular. The specification and figures discuss and demonstrate what the tag sequence does hybridize (i.e., the tag complement). As noted by MPEP 2173.05(i),

“Any negative limitation or exclusionary proviso must have basis in the original disclosure. See *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983) *aff’d* mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement.”

Since no basis has been identified, the claims are rejected as incorporating new matter. Claims 2-12 are rejected herein because they depend from claim 1 and thereby include all of the limitations of claim 1, including the subject matter designated as new matter.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim Rejections - 35 USC § 102

6. Claims 1, 2, 3, 5, 8, 9, 10, 11, and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Grossman *et al.* (US 5514543).

Grossman *et al.* (US 5514543) teach a composition comprising:

a first complex comprising a first probe comprising a first target specific portion for sequence specific hybridization to a first target nucleic acid, and a first tag; and a first mobility modifier comprising a first tail and a first tag complement for binding the first tag and

a second complex comprising a second probe comprising a second target specific portion for sequence specific hybridization to a second target nucleic acid, and a second tag; and a second mobility modifier comprising a second tail and a second tag complement for binding the second tag,

wherein a mobility of the first complex in a mobility-dependent analysis technique is distinguishable from a mobility of the second complex in the mobility-dependent analysis technique; and wherein the first complex and the second complex are present in a mixture. For an example of the basic structure of the complexes, see, for example, Figure 1A. The polynucleotide marked (22) is the tag complement. The portion marked (27) is the tail, which is made of a polymer, for example polyethylene oxide or a polypeptide chain (Col. 3, lines 59-61). The portion marked (24) is the tag (in this case shown bound to the tag complement). The portion of (26) which is not hybridized to the tag complement is the target specific portion, and this portion would inherently comprise a 3'-hydroxyl group. Grossman *et al.* teach that their method is for the detection of a "plurality of selected target sequences (Col. 3, line 1)" and thus, a plurality of these complexes would exist in a mixture.

Grossman *et al.* exemplify a tag and tag complement which comprise the sequence TCC (Fig. 4A). The compositions taught by Grossman *et al.* include probe elements attached to a polymer chain which imparts a distinctive electrophoretic mobility in a sieving matrix to the associated probe pair (Col. 3, lines 6-10). In one embodiment the compositions taught by

Art Unit: 1655

Grossman *et al.* include tails made of polyethyleneoxide units (Col. 8, lines 33-34).

Furthermore, Grossman *et al.* teach compositions which include hybridization enhancers, such as magnesium chloride (Col. 28, line 40, for example).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grossman *et al.* (US 5514543) in view of Buchardt *et al.* (Trends in Biotechnology (1993) 11(9):384-6).

Grossman *et al.* teach a composition comprising:

a first complex comprising a first probe comprising a first target specific portion for sequence specific hybridization to a first target nucleic acid, and a first tag; and a first mobility modifier comprising a first tail and a first tag complement for binding the first tag and

a second complex comprising a second probe comprising a second target specific portion for sequence specific hybridization to a second target nucleic acid, and a second tag; and a second mobility modifier comprising a second tail and a second tag complement for binding the second tag,

wherein a mobility of the first complex in a mobility-dependent analysis technique is distinguishable from a mobility of the second complex in the mobility-dependent analysis technique; and wherein the first complex and the second complex are present in a mixture. For an example of the basic structure of the complexes, see, for example, Figure 1A. The

polynucleotide marked (22) is the tag complement. The portion marked (27) is the tail, which is made of a polymer, for example polyethylene oxide or a polypeptide chain (Col. 3, lines 59-61). The portion marked (24) is the tag (in this case shown bound to the tag complement). The portion of (26) which is not hybridized to the tag complement is the target specific portion, and this portion would inherently comprise a 3'-hydroxyl group. Grossman *et al.* teach that their method is for the detection of a "plurality of selected target sequences (Col. 3, line 1)" and thus, a plurality of these complexes would exist in a mixture.

Grossman *et al.* do not teach a composition in which the first tag complement portion comprises PNA.

Buchardt *et al.* teach PNA probes and teach that PNA probes were found to form very stable Watson-Crick duplexes with DNA and RNA and that the affinity for PNAs for DNA and RNA is generally higher than that of the corresponding DNA for DNA or RNA (p. 385).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have substituted PNA for the tag complement taught by Grossman *et al.* The ordinary practitioner would have been motivated to make such a combination by the teachings of both Grossman *et al.* and Buchardt *et al.* Grossman *et al.* teaches that the sequence specific binding polymer (herein designated as the tag complement portion) is "a polymer effective to bind one target nucleic acid or sequence subset with base-sequence specificity (Col. 6, lines 6-8)," and Buchardt *et al.* teach that PNA probes have such qualities. Buchardt *et al.* further teach benefits of using PNA probes in place of DNA structures, stating that "PNAs exhibit sequence-specific binding to DNA and RNA with higher affinities and specificities than unmodified DNA. They are resistant to nuclease and protease attack in

serum and cellular extracts and, thus, appear very promising as diagnostic and biomolecular probes (Abstract).”

Response to Remarks

Applicant argues that the rejections in view of Grossman et al. are overcome by the amendments, particularly because Grossman et al. does not teach a complex wherein the tag is designed so that it does not hybridize to the regions that flank the target sequence. This argument is not persuasive because the added amendment does not provide any structural limitation on the tag or the tag complement or the regions that flank the target nucleic acid. The newly added language is intended use language. It does not structurally limit the claimed complexes because the flanking target sequence to which the tag complement is designed not to hybridize is not part of the claimed complex. Applicant is attempting to define the structure of the claimed composition based on a target sequence which is not a structural limitation of the claim, it is merely a hypothetical sequence which applicant intends the claimed complexes to hybridize to. Therefore, this limitation is not limiting to the claimed product. The structures taught Grossman et al. meet all of the structural limitations provided by the claims. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

The double patenting rejection is obviated in light of the terminal disclaimer (paper number 17).

Conclusion

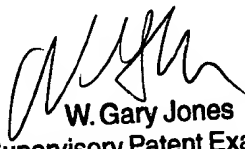
9. No claims are allowed.


10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

May 1, 2002


W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600


Juliet C Einsmann
Examiner
Art Unit 1655